SERUM HEAT STABLE ALKALINE PHOSPHATASE (HSAP) IN SOME DISORDERS OF PREGNANCY*

by
H. C. MEHTA,** M.Sc. (Hons.)
and
URMILA KAPOOR,*** M.D., D.G.O.

In search of a reliable index of placental function, obstetricians and biochemists have studied the urinary excretion of hormones Brown et al, (1959) and enzyme levels of the maternal blood Meade and Rosalki, (1963). Of all these parameters, serum heat stable alkaline phosphatase (HSAP) level has been found to be a simple and reliable index of placental function. The serum HSAP levels have been found to change progressively with the advancement of pregnancy (Hunter, 1969; Curzen and Morris, 1966; Kapoor and Mehta, 1972). Though a similar trend has been observed in cases suffering from hypertension and eclamptic toxemia during pregnancy, the serum HSAP levels in these cases were significantly higher than those in normal pregnant cases (Hunter, 1969; Kapoor and Mehta, 1973). Keeping in view the utility of this simple test in the management of pregnancy, the present study was undertaken to note the trend of HSAP levels in the following disorders of pregnancy:
(i) Anaemia
(ii) Stillbirths and abortions
(iii) Bleeding per vaginum
(iv) Cases with bad obstetric history.

Material and Methods
The following cases from the obstetric out patient department and from the obstetric ward of the Medical College Hospital, Rohtak formed the case material for the present study:
1. Sixty-five pregnant women having anaemia (Haemoglobin level less than 10.0 gms.%).
2. Five cases of stillbirths or abortions.
3. Thirty pregnant women with previous history of stillbirths or abortions.
4. Six pregnant women with complaint of bleeding per vaginum during the current pregnancy.
5. Two typical miscellaneous cases.
Serum HSAP activity was estimated by the method of King (1951) after heating the 1:1 diluted serum at 65°C for 30 minutes. The results have been expressed in King Armstrong Units (KAU).

Results and Observations

(A) Anaemic patients: Sixty-five pregnant women having anaemia were serially followed for their serum HSAP levels and 165 observations were recorded. These observations are exclusive of the HSAP levels when these patients had

*This study was conducted with grant in aid from the I.C.M.R., New Delhi.
**Demonstrator, Department of Biochemistry.
***Assistant Professor, Department of Obstetrics and Gynaecology, Medical College and Hospital, Rohtak (Haryana).

Received for publication on 28-5-1974.
attained normal haemoglobin levels after treatment for anaemia. The observations have been presented in Table I and in the scatter diagram (Fig. 1).

(B) Stillbirths and abortions: Serum HSAP levels in 5 cases who delivered stillborn babies or aborted are given below. These cases were otherwise normal and raised HSAP levels were noted before abortion or stillbirth.

Case No. SBA 1: Age 22 years, primigravida; serum HSAP levels were 3.0 KAU (22 wks) and 33.7 KAU (30 wks). Result was stillbirth.

Case No. SBA 2: Age 28 years, 3rd gravida; serum HSAP levels were 14.3 KAU (32 wks) and 25.3 KAU (36 wks). Patient delivered a dead baby.

Case No. SBA 3: Age 27 years, 3rd gravida; serum HSAP activity was 10.3 KAU at 30 weeks of gestation and 26.0 KAU at 36 weeks of gestation. Patient delivered a stillborn baby.

Case No. SBA 4: Age 24 years, primi-gravida; serum HSAP levels were 1.5 KAU (12 wks), 1.5 KAU (16 wks), 3.0 KAU (20 wks), 3.0 KAU (22 wks), 3.0 KAU (24 wks), 3.0 KAU (26 wks), 3.0 KAU (28 wks), 3.0 KAU (30 wks), 3.0 KAU (32 wks), 3.0 KAU (34 wks), 3.0 KAU (36 wks), 3.0 KAU (38 wks), 3.0 KAU (40 wks)

TABLE I
Serum HSAP Levels in Anaemic Pregnant Cases

<table>
<thead>
<tr>
<th>Gestation Period (weeks)</th>
<th>HSAP levels (KAU) in anaemic Pregnant cases</th>
<th>Number of observations</th>
<th>HSAP levels (KAU) in normal pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± S.D.</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>1.4—2.1</td>
<td>1.38 ± 0.35</td>
<td>4</td>
</tr>
<tr>
<td>18</td>
<td>1.4—2.5</td>
<td>1.90 ± 0.47</td>
<td>4</td>
</tr>
<tr>
<td>20</td>
<td>2.31 ± 0.52</td>
<td>2.31 ± 0.92</td>
<td>8</td>
</tr>
<tr>
<td>22</td>
<td>3.13 ± 0.78</td>
<td>3.13 ± 0.78</td>
<td>6</td>
</tr>
<tr>
<td>24</td>
<td>2.95 ± 1.25</td>
<td>2.95 ± 1.25</td>
<td>12</td>
</tr>
<tr>
<td>26</td>
<td>4.47 ± 1.51</td>
<td>4.47 ± 1.51</td>
<td>12</td>
</tr>
<tr>
<td>28</td>
<td>6.06 ± 2.94</td>
<td>6.06 ± 2.94</td>
<td>17</td>
</tr>
<tr>
<td>30</td>
<td>7.93 ± 1.55</td>
<td>7.93 ± 1.55</td>
<td>12</td>
</tr>
<tr>
<td>32</td>
<td>9.87 ± 3.56</td>
<td>9.87 ± 3.56</td>
<td>18</td>
</tr>
<tr>
<td>34</td>
<td>11.12 ± 2.82</td>
<td>11.12 ± 2.82</td>
<td>18</td>
</tr>
<tr>
<td>36</td>
<td>12.68 ± 4.06</td>
<td>12.68 ± 4.06</td>
<td>20</td>
</tr>
<tr>
<td>38</td>
<td>15.40 ± 4.10</td>
<td>15.40 ± 4.10</td>
<td>12</td>
</tr>
<tr>
<td>40</td>
<td>17.67 ± 4.06</td>
<td>17.67 ± 4.06</td>
<td>22</td>
</tr>
</tbody>
</table>

* HSAP values in normal cases have been referred from a previous study (Kapoor and Mehta, 1972 and 1973).

The difference between the HSAP values of normal and anaemic cases are nonsignificant (p more than 0.05) at all stages of gestation.
KAU (20 wks), 6.7 KAU (25 wks), 6.9 KAU (32 wks) and 30.0 KAU (38 weeks). Result was stillbirth.

Case No. SBA: Age 21 years, 1st gravida; serum HSAP was 18.7 KAU at 26 weeks of gestation and the patient aborted.

(C) Cases with History of abortions: Serum HSAP levels in 14 cases having history of previous abortions are recorded in Table II. In most of these cases the serum HSAP levels are in the normal range, though in 4 cases the levels were abnormal at some stage of the pregnancy indicating abnormal placental function and abortion or stillbirth was the result in these 4 cases.

(D) Cases having history of stillbirths: Serum HSAP levels of 16 cases with history of previous stillbirths are presented in Table III. Abnormal HSAP levels were recorded in 5 cases with failing placental function and these cases either aborted or delivered dead babies.

(E) History of bleeding per vaginam during the current pregnancy: Six cases with complaint of bleeding during the present pregnancy are briefly discussed below:
Case No. B1: Aged 31 years, primigravida, had bleeding for three weeks in the third month of pregnancy. Serum HSAP activity of 28 weeks was 6.2 KAU and at 32 weeks it was 6.7 KAU. The delivery was normal.

Case No. B2: Aged 25 years, 3rd gravida, had bleeding for about a week in fourth and sixth months of pregnancy. Serum HSAP levels were 2.3 KAU (28 wks), 2.7 KAU (22 wks), 3.4 KAU (26 wks), 8.6 KAU (29 wks), 10.5 KAU (34 wks) and 15.4 KAU (37 wks). The patient delivered a normal baby.

Case No. B3: Aged 30 years, fourth gravida, complained of bleeding for about 10 days during the 5th month of pregnancy. The serum HSAP activity was 1.2 KAU at 22nd week and 2.1 KAU at 26th week. The rest of the gestation period was uneventful and the patient delivered normally at home.

Case Nos. B4, B5 and B6: In these cases aged 30 years (fourth gravida), 40 years (sixth gravida) and 22 years (primigravida), bleeding was noted for about a week prior to labour. The respective HSAP values in these cases were 11.0 KAU (36 wks), 15.5 KAU (38 wks) and 15.5 KAU (34 wks). All these cases delivered normal babies.

In all these cases the serum HSAP levels were in the normal range and the deliveries as well as placentae were normal.

(F) Two Miscellaneous cases: In 2 cases, encountered during the present work, the serum HSAP levels did not show a progressive rise with the advancement of pregnancy. The serum HSAP values were as follows:

Case 1: 1.7 KAU (24 wks), 2.0 KAU (30 wks), 2.3 KAU (34 wks) and 2.2 KAU (prior to labour).

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs.)</th>
<th>Number of stillbirths</th>
<th>Length of gestation (weeks)</th>
<th>HSAP Values (K.A.U.)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>33</td>
<td>2</td>
<td>27</td>
<td>16.3</td>
<td>Dead foetus &amp; placenta with infarcts.</td>
</tr>
<tr>
<td>S2</td>
<td>42</td>
<td>2</td>
<td>24, 30, 38</td>
<td>4.2, 8.7, 15.2</td>
<td>-do-</td>
</tr>
<tr>
<td>S3</td>
<td>22</td>
<td>2</td>
<td>24, 30, 38</td>
<td>8.7, 17.8</td>
<td>-do-</td>
</tr>
<tr>
<td>S4</td>
<td>26</td>
<td>2</td>
<td>28, 38</td>
<td>13.3</td>
<td>-do-</td>
</tr>
<tr>
<td>S5</td>
<td>22</td>
<td>2</td>
<td>38</td>
<td>18.0</td>
<td>-do-</td>
</tr>
<tr>
<td>S6</td>
<td>34</td>
<td>1</td>
<td>22, 23, 24</td>
<td>3.5, 6.2, 14.6</td>
<td>-do-</td>
</tr>
<tr>
<td>S7</td>
<td>21</td>
<td>2</td>
<td>28, 38, 40</td>
<td>5.2, 10.7, 25.3</td>
<td>-do-</td>
</tr>
<tr>
<td>S8</td>
<td>25</td>
<td>2</td>
<td>38</td>
<td>16.0</td>
<td>-do-</td>
</tr>
<tr>
<td>S9</td>
<td>30</td>
<td>2</td>
<td>38</td>
<td>16.7, 16.5, 17.2</td>
<td>-do-</td>
</tr>
<tr>
<td>S10</td>
<td>23</td>
<td>1</td>
<td>38</td>
<td>14.3</td>
<td>-do-</td>
</tr>
<tr>
<td>S11</td>
<td>38</td>
<td>3</td>
<td>38</td>
<td>9.3, 16.5</td>
<td>-do-</td>
</tr>
<tr>
<td>S12</td>
<td>30</td>
<td>2</td>
<td>38</td>
<td>17.8</td>
<td>-do-</td>
</tr>
<tr>
<td>S13</td>
<td>22</td>
<td>2</td>
<td>38</td>
<td>-do-</td>
<td></td>
</tr>
<tr>
<td>S14</td>
<td>24</td>
<td>1</td>
<td>38</td>
<td>-do-</td>
<td></td>
</tr>
<tr>
<td>S15</td>
<td>21</td>
<td>2</td>
<td>38</td>
<td>-do-</td>
<td></td>
</tr>
<tr>
<td>S16</td>
<td>29</td>
<td>2</td>
<td>38</td>
<td>-do-</td>
<td></td>
</tr>
</tbody>
</table>
Recurrent Vesical Calculus in Association with Prolapse—Patharajaian and Prvathamma pp. 175-177

Fig. 1
Shows bladder descent and calculi filling the cystocele.

Fig. 2
Shows the phosphatic stones removed from the same.

Some Special Aspects of Malignant Trophoblastic Disease—Chakravarty et al. pp. 178-181

Fig. 1
(H & E sections x 100) Atypical proliferation of chorionic epithelium (Case No. 1)

Fig. 2
(H & E sections x 100) chorioadenoma destruens (Case No. 1)
Photograph showing the gross appearance of the two tumours, multilobular in type with glistening surface.

H & E x 300 Microphotograph showing bundles of cells having fusiform and long tapering type of nuclei with intervening zones of dense collagenous tissue.

Diagram showing uterus didelphys with gynatrasia on the left side. Normal menstruation was occurring from the right side.
Fig. 1
Shows focal round cell infiltration.

Fig. 2
Shows focal necrosis.

Fig. 3
Shows cellular necrosis.

Fig. 4
Dilated vein with lymphocytes, cellular debris and platelets.
Tuberculous Endometritis—Prabhakar et al. pp. 117-122

Fig. 1
Photomicrograph showing vacuolar inclusions inside the giant cells.

Fig. 2
Photomicrograph showing calcific spherule inside the giant cell.

Congenital Chickenpox—Pragna and Soneji
pp. 144-145

Fig. 3
Photomicrograph showing a foreign body giant cell and lymphocytes surrounding the granuloma.

Fig. 1
New born baby showing typical rash of chickenpox.
Fig. 1
Nuclei and nucleoli of a gland of the normal proliferative endometrium of the control group.

Fig. 2
Nuclei and nucleoli of a gland of the proliferative endometrium with IUCD.

Fig. 3
Nuclei and nucleoli of a gland of the normal secretory endometrium.

Fig. 4
Nuclei and nucleoli of a gland of the secretory endometrium with IUCD.
Congenital Atresia of Vagina & Fusion of Mullerian Ducts—Chakravarty et al. pp. 99-104

Fig. 2
Photograph showing finding on laparotomy in a case of congenital absence of vagina. Two rudimentary uteri connected by a fibromuscular band, normal tubes and ovaries on either side are the usual findings.

Fig. 3
Diagramatic representation of the laparotomy findings in a case of atresia.

Fig. 4
Intravenous pyelogram showing double kidney with single ureter on right side with absence of kidney and ureter on the left side in a case of congenital absence of vagina.

Fig. 5
Photomicrograph showing structure of corpus luteum in the ovary in a case of congenital absence of vagina.
Fig. 5
Effect of PGE, on upper segment pregnant myometrium (Mid trimester).

Fig. 6
Effect of PGE, on lower segment pregnant myometrium (Term pregnancy).

Fig. 7
Effect of PGF, alpha on lower segment pregnant myometrium (Term Pregnancy).

Fig. 1
Photograph showing congenital absence of vagina.

Congenital Atresia of Vagina & Fusion of Mullerian Ducts—Chakravarty et al. pp. 99-104
Fig. 1
Effect of PGE\textsubscript{1} and PGF\textsubscript{1\alpha} on upper segment pregnant myometrium (1st trimester).

Fig. 2
Effect of PGE\textsubscript{1}, PGF\textsubscript{1\alpha} and Ergometrine on upper segment pregnant myometrium (Term pregnancy).

Fig. 3
Effect of PGE\textsubscript{1} and PGF\textsubscript{1\alpha} on upper segment pregnant myometrium (Term pregnancy).

Fig. 4
Effect of PGF\textsubscript{1\alpha} and Ergometrine on upper segment pregnant myometrium (Mid trimester).
**Fig. 1**
Photomicrograph of the fertilised ovum H & E x 10.

**Fig. 2**
Photomicrograph showing primordial villi and placental site giant cells. H & E x 100.

**Fig. 3**
Photomicrograph showing the details of the embryonic disc. H & E x 100.

*Sponaneous Annular Detachment of the Cervix — Kawathekar and Gampuohit pp. 141-143*

**Fig. 1**
Shows the annularly detached cervix.
Uterus Didelphys with Unilateral Haematoccolpos—Raut pp. 170-171

Fig. 1
Gross appearance of the uterus along with bilateral ovarian tumours.

Fig. 2
Microphotograph of Krukenberg tumour showing the signet cells.
Cases 2: 2.3 KAU (26 wks), 2.2 KAU (30 wks), 2.7 KAU (35 wks) and 2.8 KAU (38 wks).

These observation are contrary to the normal trend, specially when in both the cases the gestation period was uneventful and deliveries were also normal. No infarcts on placenta were noted.

Discussion

Serum HSAP levels have been found to rise progressively with the advancing gestation. Similar trend has been noted in normal pregnancy as well as in that complicated by hypertensive disorders, but the levels of serum HSAP in the latter case are significantly higher than those in normal pregnancy (Hunter, 1969; Kapoor and Mehta, 1973) at all stages of gestation.

In the present study serum HSAP levels in anaemic pregnant patients have been found to be in the same range as observed for normal pregnancy. Since HSAP levels have been assumed to reflect the state of placenta, the normal HSAP levels in the anaemic (but otherwise normal) pregnant cases point towards the nondamaging effect of anaemia only on the placenta. This is supported by the observation that the placenta was normal in all the cases having normal HSAP levels and the delivered babies too were normal.

The serum HSAP levels in cases of bad obstetric history varied with the individuals. In some of these cases (A1, A2, A3, A6 and S1 to S5) and others in which the present pregnancy terminated in stillbirths or abortions (SBA1 to SBA5), the serum HSAP levels were found to be abnormally high at some (or more) stage of gestation. In rest of the cases, including those with complaints of bleeding during the present pregnancy, the serum HSAP levels were in the normal range throughout the gestation period and the patients delivered normally. The placentae were degenerated in the former cases (having high HSAP levels), while these were intact in the latter cases (having low HSAP values), an observation lending further support to the value of serum HSAP as an index of placental function.

The persistent low levels of serum HSAP in 2 cases of the present study are, however, difficult to explain, specially when whole of the gestation period of these 2 cases was uneventful and the delivered babies and placentae were also normal. One possibility may be the decreased synthesis of the enzyme by the placental cells without affecting the morphological or functional state of the placenta.

To conclude, the study of serum HSAP levels in normal pregnancy, hypertensive disorders of pregnancy and other disorders of pregnancy has indicated that the serum HSAP levels provide a reliable index of placental function and can be depended upon in the management of pregnancy. As already pointed out, it is possible to lay down a critical value for serum HSAP activity at any period of gestation because of a wide scatter. The serum HSAP levels should be assessed at regular convenient intervals and any abrupt rise or abnormally high value, compared to the normal values, be taken note of.

Summary

Serum heat stable alkaline phosphatase (HSAP) levels have been studied in 65 pregnant women having anaemia, in 5 cases leading to stillbirth or abortions, in 30 pregnant cases with bad obstetric history, in 6 pregnant cases with comp-
laints of bleeding during the current pregnancy and in 2 miscellaneous cases. The serum HSAP levels in anaemic (but otherwise normal) cases were found to be in the same range as observed for normals. The serum HSAP levels in cases of bad obstetric history corresponded well to the condition of placenta, being normal in cases with normal placental function and abnormal in others with failing placental function. The serum HSAP levels in case of all pregnancies leading to stillbirth or abortion were abnormally elevated at some stage of gestation. In two cases, however, the serum HSAP levels remained persistently low throughout the gestation period, though the gestation period was uneventful and the delivered babies were also normal. This might be due to lowered synthesis of the enzyme by the placental cells. In all, serum HSAP levels have been found to provide a reliable test for placental function in the management of pregnancies.

References